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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,874	11/03/2003	Arthur Kunz	P194 1011.1	4900

67327 7590 06/02/2011

WOMBLE CARLYLE SANDRIDGE & RICE, PLLC
ATTN: IP DOCKETING
PO BOX 7037
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EXAMINER	
XIAO, YAN	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
06/02/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPDocketing@WCSR.COM

Office Action Summary	Application No.	Applicant(s)
	10/699,874	KUNZ ET AL.
	Examiner	Art Unit
	YAN XIAO	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *150-152, 158-164, 167-174, 181-187, 190-210, 213-221, 227-233 and 236-251* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/25/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 150-152,158-164,167-174,181-187,190-210,213-221,227-233 and 236-251.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/25/2010 has been entered.

Claims 150-152, 158-164, 167-174, 181-187, 190-210, 213-221, 227-233 and 236-251 are pending and under consideration.

Specification

2. The disclosure is objected to because the examples are misnumbered, i.e. Example 7 in the specification is missing.

Appropriate correction is required.

Claim Objections

3. The amendment to the claims filed on 03/08/2010 does not comply with the requirements of 37 CFR 1.121(c) because it does not include a complete listing of all claims, i.e. cancelled claims 259-268. Amendments to the claims filed on or after July 30, 2003 must comply with 37 CFR 1.121(c) which states:

(c) *Claims*. Amendments to a claim must be made by rewriting the entire claim with all changes (*e.g.*, additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim,

cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(1) *Claim listing.* All of the claims presented in a claim listing shall be presented in ascending numerical order. Consecutive claims having the same status of "canceled" or "not entered" may be aggregated into one statement (*e.g.*, Claims 1–5 (canceled)). The claim listing shall commence on a separate sheet of the amendment document and the sheet(s) that contain the text of any part of the claims shall not contain any other part of the amendment.

(2) *When claim text with markings is required.* All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of "currently amended," and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of "currently amended," or "withdrawn" if also being

amended, shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as "withdrawn—currently amended."

(3) *When claim text in clean version is required.* The text of all pending claims not being currently amended shall be presented in the claim listing in clean version, *i.e.*, without any markings in the presentation of text. The presentation of a clean version of any claim having the status of "original," "withdrawn" or "previously presented" will constitute an assertion that it has not been changed relative to the immediate prior version, except to omit markings that may have been present in the immediate prior version of the claims of the status of "withdrawn" or "previously presented." Any claim added by amendment must be indicated with the status of "new" and presented in clean version, *i.e.*, without any underlining.

(4) *When claim text shall not be presented; canceling a claim.*

(i) No claim text shall be presented for any claim in the claim listing with the status of "canceled" or "not entered."

(ii) Cancellation of a claim shall be effected by an instruction to cancel a particular claim number. Identifying the status of a claim in the claim listing as "canceled" will constitute an instruction to cancel the claim.

(5) *Reinstatement of previously canceled claim.* A claim which was previously canceled may be reinstated only by adding the claim as a "new" claim with a new claim number.

Drawings

4. The replacement drawing of Figure 6 was received on 08/09/2009. This drawing is accepted.

The drawings are objected to because the numbering of the VL chain in Figure 5 appears to be incorrect. In particular, the position labeled "40" appears to amino acid number 45 when compared to SEQ ID NO: 7. similarly, there numbering appears to be shifted on the rest of the VL chain. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 200-203 and 244-247 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the anti-CD22 antibody comprises a heavy chain framework residue selected from one or more of positions 1, 28, 48, 72, and 97 (linear numbering) of SEQ ID NO:8 occupied by Glu, Arg, Ile, Ala, and Thr, respectively, wherein the remainder of the heavy chain framework is occupied by corresponding residues of the human acceptor framework of SEQ ID NO: 21 **and** 22, the anti-CD22 antibody comprises a light chain framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) of SEQ ID NO:7 occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework is occupied by corresponding residues of the human acceptor framework of SEQ ID NO: 17 **and** 18, *does not* reasonably provide enablement for the anti-CD22 antibody comprises a heavy chain framework residue selected from one or more of positions 1, 28, 48, 72, and 97 (linear numbering) of SEQ ID NO:8 occupied by Glu, Arg, Ile, Ala, and Thr, respectively, wherein the remainder of the heavy chain framework is occupied by corresponding residues of the human acceptor framework of SEQ ID NO: 21 **or** 22, the anti-CD22 antibody comprises a light chain framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) of SEQ ID NO:7 occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework is occupied by corresponding residues of the human acceptor framework of SEQ ID NO: 17 **or** 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims 200-203 and 244-247 are drawn to a method of claim 198 or 242, wherein the anti-CD22 antibody comprises a heavy chain framework residue selected from one or more of positions 1, 28, 48, 72, and 97 (linear numbering) of SEQ ID NO:8 occupied by Glu, Arg, Ile, Ala, and Thr, respectively, wherein the remainder of the heavy chain framework region is occupied by corresponding residues of the human acceptor framework of SEQ ID NO: 21 or 22; a method of claim 198 or 242, wherein the anti-CD22 antibody comprises a light chain framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) of SEQ ID NO:7 occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework region is occupied by corresponding residues of the human acceptor framework of SEQ ID NO: 17 or 18.

> The specification teaches:
> the human framework region of SEQ ID NOs 17 or 18 or 21 or 22 are partial human framework region. See Figures 5-6.

One of skill in the art cannot extrapolate the teachings of the specification to enable the scope of the claims because a CD22 antibody comprising a light chain framework region of SEQ ID NOs 17 or 18 or a heavy chain framework region of SEQ ID NOs: 21 or 22 reads on antibodies comprising partial human framework regions, i.e. incomplete antibodies.

The methods generation of a humanized antibody is well known in the art, for example, Kashmiri et al. (Methods 2005, 36:25–34) teaches that humanization of an antibody by specificity determining residues (SDR) grafting requires the transfer of only some of the CDR residues to a human scaffold. Thus, SDR grafting generates a humanized antibody with a substantially reduced number of non-human residues than those present in its CDR-grafted counterpart. Both the SDR and CDR grafting procedures require selection of the most appropriate human frameworks to be used as templates, and identification of the framework residues that are critical to the preservation of the structure of the antigen-binding site. The framework sequences of the humanized antibody are largely contributed by the human templates. When comparing the sequences of the frameworks of the target and the template antibodies, if any of the crucial residues of the target antibody is found to be different from their corresponding residues in the human template, the crucial residues of the target antibody are incorporated in the frameworks of the templates for the final design of the humanized antibody. For humanization by SDR grafting, only the SDRs of the target antibody are transferred to the human scaffold; the non-SDRs of the human template are included in the final construct. To that end, the CDR sequences of the template and target antibodies are compared and the positions where they differ are marked. It is then determined whether the positions where the template and target CDRs differ are the ligand-contact positions. All the residues of the target antibody that are identified as

SDRs are transferred to the human template framework. For a non-SDR position, if the residue in the target antibody differs from the corresponding residue in the human template, the human residue is incorporated in the final construct. See right col. of page 26. Kashmiri et al. teach that the most crucial step in humanization of an antibody is the choice of the most appropriate framework regions, which encompasses four framework domains (FR1-4) surrounding the CDR domains. See paragraph p. 26 and 27 and Fig. 1. Additionally, Gussow et al. (1991, Methods in Enzymology 203:99-121) is relevant to the instant rejection. Gussow et al. specifically teaches that the applicability of antibody humanization techniques relies on, among others, the assumption that the frameworks of the variable domains serve as a scaffold to support the CDRs in a specific way that facilitates antigen binding and further teach that it is of great importance to retain the interactions between the donor CDRs and the acceptor framework as closely as possible to the CDR-framework interactions of the original Mab. Gussow et al. further teaches that the affinity of the first fully humanized antibody CAMPATH1 was nearly 40 fold lower compared to the original rat MAb, apparently because of differences of residues in the framework region of the humanized antibody compared to those of the original antibody, particularly those located close to the CDRs. Clearly, alteration of even one amino acid residue can alter the packing of the residues within the molecule as it was demonstrated that mutation of the human Ser 27 to a Phe (the residue found in the original rat antibody at this position) restored the binding affinity of the humanized antibody close to the original affinity (see page 100). Clearly, given the sensitivity of antibodies to even a single amino acidealteration, one could not predict that an antibody comprising only a single framework would function as claimed. Furthermore, Wu et al. (J. Mol. Biol. (1999) 294, 151-162) teach that it is difficult to predict

which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding (page 152 left col.) but certain residues have been identified as important for maintaining conformation.

Thus, given that the art teaches the importance of framework selection in antibody humanization and the claims encompass antibodies with only a single framework domain in the VL and/or VH domain, in absence of further guidance or exemplification, undue experimentation would be required for one of skill in the art to make and/or use the invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 150-152, 158-164, 167-174, 181-187, 190-210, 213-221, 227-233 and 236-251 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 210-214 application No. 10/428,894 in view of Tsai et al. (Clin Lymphoma. 2000 Jun;1(1):62-66, hereafter Tsai) and in view of Press et al. (Hematology Am Soc Hematol Educ Program. 2001:221-40, hereafter Press). Although the claims are not identical, they are not patentably distinct from each other because application No. 10/428,894 teaches a N-acetyl-gamma calicheamicin DMH-anti-CD22 antibody conjugate comprising SEQ ID NO: 1 for CDR-H1, residues 50-66 SEQ ID NO: 27 for CDR-H2, SEQ ID NO: 3 for CDR-H3, SEQ ID NO: 4 for CDR-L1, SEQ ID NO: 5 for CDR-L2, SEQ ID NO: 6 for CDR-L3, or the VL of SEQ ID NO:19 and the VH of SEQ ID NO: 27, or the VL of SEQ ID NO: 28 and the VH of SEQ ID NO: 30 , see claims 210-214. SEQ ID NOs: 1, 27, 3, 4, 5, and 6 of Application No. 10/428,894 are 100% identical with SEQ ID NOs: 1, 27, 3, 4, 5, and 6 of instant case. See alignments below. Tsai teaches a method of treating B-cell malignancy patients using CHOP,

rituximab and anti-CD22, see abstract, pages 63-64. Press teaches combination of Rituximab with chemotherapy (CHOP, DHAP, CVP) in B-cell malignancy, see abstract, left col. of page 226 through right col. of page 228. Press teaches intravenous administration of rituximab. See p. 222-2nd col.

Thus, it would have been *prima facie* obvious to combine the teachings of application No. 10/428,894 with that of Tsai and Press, because the application No. 10/428,894 teaches the N acetyl-gamma calicheamicin DMH-anti-CD22 antibody conjugate comparing SEQ ID NO: 1 for CDR-H1, residues 50-66 SEQ ID NO: 27 for CDR-H2, SEQ ID NO: 3 for CDR-H3, SEQ ID NO: 4 for CDR-L1, SEQ ID NO: 5 for CDR-L2, SEQ ID NO: 6 for CDR-L3, Tsai teaches a method of treating B-cell malignancy patients using CHOP, rituximab and anti-CD22, Press teaches the combination of Rituximab with chemotherapy in B-cell malignancy. Thus, one of skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of the application No. 10/428,894 with that of Tsai and Press to treat B-cell malignancy patients using the calicheamicin derivative-anti-CD22 antibody conjugate combined with rituximab and a chemotherapeutic agent, because of the benefits and advantages of the treatment can improve overall response and survivals rates.

It is noted that 35 USC § 121 does not provide protection for continuation or continuation in-part applications, and this application is a continuation in part of application No. 10/428,894. See 92 USPQ2d 1289 *Amgen Inc. v. F. Hoffmann-La Roche Ltd.* (Fed. Cir. 2009) and *Pfizer, Inc. v. Teva* Pharmaceuticals USA, Inc. 518 F.3d 1353 (Fed. Cir. 2008).

All other rejections and objections set forth in the Office Action of 11/25/2009 are withdrawn.

5. No claims allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YAN XIAO whose telephone number is (571)270-3578. The examiner can normally be reached at 7:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, Primary Examiner, Peter Reddig (571-272-9031), or the examiner's supervisor, Misook Yu (571-272-0839) can be reached. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/YAN XIAO/
Examiner, Art Unit 1642

/PETER J REDDIG/
Primary Examiner, Art Unit 1642

APPENDIX

US-10-428-894-1

; Sequence 1, Application US/10428894
; Publication No. US20040082764A1
; GENERAL INFORMATION:
; APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
; TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
; FILE REFERENCE: AM100788
; CURRENT APPLICATION NUMBER: US/10/428,894
; CURRENT FILING DATE: 2003-05-02
; NUMBER OF SEQ ID NOS: 51
; SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 1
; LENGTH: 5
; TYPE: PRT
; ORGANISM: mouse
; FEATURE:
; OTHER INFORMATION: 5/44g CDR-H1
; FEATURE:
; NAME/KEY:
US-10-428-894-1

Query Match 100.0%; Score 5; DB 4; Length 5;
Best Local Similarity 100.0%;
Matches 5; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 NYWIH 5
              |||||
Db          1 NYWIH 5
```

US-10-428-894-2
; Sequence 2, Application US/10428894
; Publication No. US20040082764A1
; GENERAL INFORMATION:
; APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
; TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
; FILE REFERENCE: AM100788
; CURRENT APPLICATION NUMBER: US/10/428,894
; CURRENT FILING DATE: 2003-05-02
; NUMBER OF SEQ ID NOS: 51
; SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 2
; LENGTH: 17
; TYPE: PRT
; ORGANISM: mouse
; FEATURE:
; OTHER INFORMATION: mouse monoclonal 5/44 CDR-H2gL1 T3
; FEATURE:
; NAME/KEY:
US-10-428-894-2

Query Match 100.0%; Score 17; DB 4; Length 17;
Best Local Similarity 100.0%;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 GINPGNNYTTYKRNLKG 17
              |||||||||||||||||
Db          1 GINPGNNYTTYKRNLKG 17
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US-10-428-894-27
; Sequence 27, Application US/10428894
; Publication No. US20040082764A1
; GENERAL INFORMATION:

```
;  APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
;  TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
;  FILE REFERENCE: AM100788
;  CURRENT APPLICATION NUMBER: US/10/428,894
;  CURRENT FILING DATE:  2003-05-02
;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 27
;   LENGTH: 121
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: gH7
;   FEATURE:
;   NAME/KEY:
US-10-428-894-27

  Query Match             100.0%;  Score 121;  DB 4;  Length 121;
  Best Local Similarity   100.0%;
  Matches  121;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVQLVQSGAEVKKPGASVKVSCKASGYRFTNYWIHWVRQAPGQGLEWIGGINPGNNYATY 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 EVQLVQSGAEVKKPGASVKVSCKASGYRFTNYWIHWVRQAPGQGLEWIGGINPGNNYATY 60

Qy         61 RRKFQGRVTMTADTSTSTVYMELSSLRSEDTAVYYCTREGYGNYGAWFAYWGQGTLVTVS 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 RRKFQGRVTMTADTSTSTVYMELSSLRSEDTAVYYCTREGYGNYGAWFAYWGQGTLVTVS 120

Qy        121 S 121
              |
Db        121 S 121



US-10-428-894-3
; Sequence 3, Application US/10428894
; Publication No. US20040082764A1
; GENERAL INFORMATION:
;  APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
;  TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
;  FILE REFERENCE: AM100788
;  CURRENT APPLICATION NUMBER: US/10/428,894
;  CURRENT FILING DATE:  2003-05-02
;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 3
;   LENGTH: 12
;   TYPE: PRT
;   ORGANISM: mouse
;   FEATURE:
;   OTHER INFORMATION: mouse monoclonal 5/44 CDR-H3
;   FEATURE:
;   NAME/KEY:
US-10-428-894-3

  Query Match             100.0%;  Score 12;  DB 4;  Length 12;
  Best Local Similarity   100.0%;
  Matches   12;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EGYGNYGAWFAY 12
              ||||||||||||
Db          1 EGYGNYGAWFAY 12


US-10-428-894-4
; Sequence 4, Application US/10428894
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```
; Publication No. US20040082764A1
; GENERAL INFORMATION:
;  APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
;  TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
;  FILE REFERENCE: AM100788
;  CURRENT APPLICATION NUMBER: US/10/428,894
;  CURRENT FILING DATE:  2003-05-02
;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 4
;   LENGTH: 16
;   TYPE: PRT
;   ORGANISM: mouse
;   FEATURE:
;   OTHER INFORMATION: mouse monoclonal 5/44 CDR-L1
;   FEATURE:
;   NAME/KEY:
US-10-428-894-4

  Query Match             100.0%;  Score 16;  DB 4;  Length 16;
  Best Local Similarity   100.0%;
  Matches   16;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 RSSQSLANSYGNTFLS 16
              ||||||||||||||||
Db          1 RSSQSLANSYGNTFLS 16


US-10-428-894-5
; Sequence 5, Application US/10428894
; Publication No. US20040082764A1
; GENERAL INFORMATION:
;  APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
;  TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
;  FILE REFERENCE: AM100788
;  CURRENT APPLICATION NUMBER: US/10/428,894
;  CURRENT FILING DATE:  2003-05-02
;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 5
;   LENGTH: 7
;   TYPE: PRT
;   ORGANISM: mouse
;   FEATURE:
;   OTHER INFORMATION: mouse monoclonal 5/44 CDR-L2
;   FEATURE:
;   NAME/KEY:
US-10-428-894-5

  Query Match             100.0%;  Score 7;  DB 4;  Length 7;
  Best Local Similarity   100.0%;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GISNRFS 7
              |||||||
Db          1 GISNRFS 7


US-10-428-894-6
; Sequence 6, Application US/10428894
; Publication No. US20040082764A1
; GENERAL INFORMATION:
;  APPLICANT: WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.
;  TITLE OF INVENTION: CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
;  FILE REFERENCE: AM100788
;  CURRENT APPLICATION NUMBER: US/10/428,894
;  CURRENT FILING DATE:  2003-05-02
```

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;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 6
;   LENGTH: 9
;   TYPE: PRT
;   ORGANISM: mouse
;   FEATURE:
;   OTHER INFORMATION: mouse monoclonal 5/44CDR-L3
;   FEATURE:
;   NAME/KEY:
US-10-428-894-6

  Query Match             100.0%;  Score 9;  DB 4;  Length 9;
  Best Local Similarity   100.0%;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LQGTHQPYT 9
              |||||||||
Db          1 LQGTHQPYT 9



US-10-428-408A-27
; Sequence 27, Application US/10428408A
; Publication No. US20030235869A1
; GENERAL INFORMATION:
;  APPLICANT: Celltech R&D Limited
;  TITLE OF INVENTION: BIOLOGICAL PRODUCTS
;  FILE REFERENCE: CARP0004-100
;  CURRENT APPLICATION NUMBER: US/10/428,408A
;  CURRENT FILING DATE:  2003-05-02
;  NUMBER OF SEQ ID NOS: 51
;  SOFTWARE: SeqWin99, version 1.02
; SEQ ID NO 27
;   LENGTH: 121
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   NAME/KEY: CHAIN
;   OTHER INFORMATION: gH7
US-10-428-408A-27

  Query Match             100.0%;  Score 121;  DB 4;  Length 121;
  Best Local Similarity   100.0%;
  Matches  121;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVQLVQSGAEVKKPGASVKVSCKASGYRFTNYWIHWVRQAPGQGLEWIGGINPGNNYATY 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 EVQLVQSGAEVKKPGASVKVSCKASGYRFTNYWIHWVRQAPGQGLEWIGGINPGNNYATY 60

Qy         61 RRKFQGRVTMTADTSTSTVYMELSSLRSEDTAVYYCTREGYGNYGAWFAYWGQGTLVTVS 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 RRKFQGRVTMTADTSTSTVYMELSSLRSEDTAVYYCTREGYGNYGAWFAYWGQGTLVTVS 120

Qy        121 S 121
              |
Db        121 S 121
```